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Ambient Water Quality Criteria: Fluoranthene

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FLUORANTHENE

Ambient Water Quality Criteria

Criteria and Standards Division
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CRITERION DOCUMENT

FLUORANTHENE

CRITERIA

Aquatic Life

For fluoranthene the criterion to protect freshwater aquatic life as derived using procedures other than the Guidelines is 250 µg/l as a 24-hour average and the concentration should not exceed 560 µg/l at any time.

For fluoranthene the criterion to protect saltwater aquatic life as derived using the Guidelines is 0.30 µg/l as a 24-hour average and the concentration should not exceed 0.69 µg/l at any time.

Human Health

For the protection of human health from the toxic properties of fluoranthene exposure through water, the ambient water quality criterion is determined to be 200 µg/l.

BIBLIOGRAPHIC INFORMATION

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Section 304(a) of the Clean Water Act (33 U.S.C. 1314(a)), requires EPA to publish and periodically update water quality criteria. These criteria are to reflect the latest scientific knowledge on the identifiable effects of pollutants on public health and welfare, aquatic life, and recreation. This report presents water quality criteria for fluoranthene. It presents concentration criteria for the protection of fresh water and saltwater aquatic life. It presents 'safe' concentrations for humans, and in the case of suspect or proven carcinogens, gives various levels of incremental cancer risk. A section 304(a) water quality criterion is a qualitative or quantitative estimate of the concentration of a water constituent or pollutant in ambient waters which, when not exceeded, will ensure a water quality sufficient to protect a specified water use. Under the Act a criterion is a scientific entity, based solely on data and scientific judgment. It does not reflect considerations of economic or technological feasibility nor is it a water quality standard and in itself has , ...

KEYWORDS: *Water quality, *Toxicology, *Water pollution effects(Humans), *Water pollution effects(Animals), *Toxic substances, *Fluoranthene, *Water pollution effects(Plants).

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Introduction

Fluoranthene, a polynuclear aromatic hydrocarbon, is produced from the pyrolytic processing of organic raw materials such as coal and petroleum at high temperatures (Andelman and Snodgrass, 1974). It is also known to occur naturally as a product of plant biosynthesis (Bornoff, et al. 1968).

Fluoranthene (1,2-benzacenaphthene, Idryl) has the molecular formula $C_{16}H_{10}$. It is further characterized by a molecular weight of 202; a melting point of 111 degrees C; a boiling point of approximately 375 degrees C and a vapor pressure of 0.01 mm Hg at 25 degrees C. It is soluble in water to the extent of 265 µg/liter (Davis, et al. 1942; Klevens, 1950).

Fluoranthene is ubiquitous in the environment and has been detected in U.S. air (Searle, 1976), in foreign and domestic drinking waters (Harrison, et al. 1975; Basu and Saxena, 1977; Noms, 1977) and in foodstuffs (Howard, et al. 1966a,b,c; Howard, et al. 1969). It is also contained in cigarette smoke (Hoffman, et al. 1972).

There is concern about the toxicity of fluoranthene because it is widespread in the human environment and belongs to a class of compounds (polynuclear aromatic hydrocarbons) that contain numerous potent carcinogens. Experimentally, fluoranthene does not exhibit properties of a mutagen or primary carcinogen but it is a potent cocarcinogen (Van Duuren and Goldschmidt, 1976; Tokiwa, et al. 1977; LaVoie,

et al. 1978). In the laboratory, fluoranthene has also demonstrated toxicity to various freshwater and marine organisms (U.S. EPA, 1978). This finding, coupled with the cocarcinogenic properties of the compound, points out the need to protect humans and aquatic organisms from the potential hazards associated with fluoranthene in water.

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AQUATIC LIFE TOXICOLOGY*

FRESHWATER ORGANISMS

Introduction

Bluegill, Daphnia magna, and the alga, Selenastrum capricornutum, have been studied using static test procedures and unmeasured concentrations. The range of LC50 and EC50 values is 3,980 to 325,000 µg/l and the bluegill is most sensitive.

Acute Toxicity

The unadjusted 96-hour LC50 value for the bluegill (U.S. EPA, 1978) is 3,980 µg/l, and after adjustment by the appropriate Guidelines factors results in the Final Fish Acute Value of 560 µg/l (Table 1).

Daphnia Magna is more resistant with a 48-hour EC50 value of 325,000 µg/l which datum results in a Final Invertebrate Acute Value of 13,000 µg/l (Table 2).

The Final Acute Value for freshwater organisms and fluoranthene is 560 µg/l.

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*The reader is referred to the Guidelines for Deriving Water Quality Criteria for the Protection of Aquatic Life [43 FR 21506 (May 18, 1978) and 43 FR 29028 (July 5, 1978)] and the Methodology Document in order to better understand the following discussion and recommendation. The following tables contain the appropriate data that were found in the literature, and at the bottom of each table are the calculations for deriving various measures of toxicity as described in the Guidelines.

Chronic Toxicity

There are no data on the chronic effects of fluoranthene on freshwater organisms.

Plant Effects

The alga, Selenastrum capricornutum, has been exposed to fluoranthene and the 96-hour EC50 values for cell number and chlorophyll a are 54,400 and 54,600 µg/l, respectively. The lower value becomes the Final Plant Value.

Residues

No measured steady-state bioconcentration factor (BCF) is available for fluoranthene. A BCF can be estimated using the calculated octanol-water partition coefficient of 79,000. This coefficient is used to derive an estimated BCF of 3,100 for aquatic organisms that contain about 8 percent lipids. If it is known that the diet of the wildlife of concern contains a significantly different lipid content, an appropriate adjustment in the estimated BCF should be made.

CRITERION FORMULATION

Freshwater - Aquatic Life

Summary of Available Data

The concentrations below have been rounded to two significant figures.

Final Fish Acute Value = 560 µg/l

Final Invertebrate Acute Value = 13,000 µg/l

Final Acute Value = 560 µg/l

Final Fish Chronic Value = not available

Final Invertebrate Chronic Value = not available

Final Plant Value = 54,000 µg/l

Residue Limited Toxicant Concentration = not available

Final Chronic Value = 54,000 µg/l

0.44 x Final Acute Value = 250 µg/l

No freshwater criterion can be derived for fluoranthene using the Guidelines because no Final Chronic Value for either fish or invertebrate species or a good substitute for either value is available.

Data for fluoranthene and saltwater organisms can be used to estimate a criterion.

For fluoranthene and saltwater organisms, 0.44 times the Final Acute Value is less than the Final Chronic Value derived from results of a life cycle test with the mysid shrimp. Therefore, a reasonable estimate of a criterion for fluoranthene and freshwater organisms would be 0.44 times the Final Acute Value.

The maximum concentration for fluoranthene is the Final Acute Value of 560 µg/l and the estimated 24-hour average concentration is 0.44 times the Final Acute Value. No important adverse effects on freshwater aquatic organisms have been reported to be caused by concentrations lower than the 24-hour average concentration.

Criterion: For fluoranthene the criterion to protect freshwater aquatic life as derived using procedures other than the Guidelines is 250 µg/l as a 24-hour average and the concentration should not exceed 560 µg/l at any time.

Table 1. Freshwater fish acute values for fluoranthene (U.S. EPA, 1978)

Organism	Bioassay Method*	Test Conc.**	Time (hrs)	LC50 (ug/l)	Adjusted LC50 (ug/l)
Bluegill, *Lepomis macrochirus*	S	U	96	3,980	2,180

* S = static

** U = unmeasured

Geometric mean of adjusted values = 2,180 ug/l $\frac{2,180}{3.9}$ = 560 ug/l

Table 2. Freshwater invertebrate acute values for fluoranthene (U.S. EPA, 1978)

Organism	Bioassay Method*	Test Conc.**	Time (hrs)	LC50 (ug/l)	Adjusted LC50 (ug/l)
Cladoceran, Daphnia magna	S	U	48	325,000	275,000

* S = static

** U = unmeasured

Geometric mean of adjusted values = 275,000 µg/l $\frac{275,000}{21}$ = 13,000 µg/l

Table 3. Freshwater plant effects for fluoranthene (U.S. EPA, 1978)

Organism	Effect	Concentration (ug/l)
Alga, *Selenastrum capricornutum*	EC50 96-hr cell numbers	54,400
Alga, *Selenastrum capricornutum*	EC50 96-hr chlorophyll *a*	54,600

Lowest plant value = 54,400 ug/l

SALTWATER ORGANISMS

Introduction

Contrary to the relationship between freshwater fish and invertebrate species, the mysid shrimp is much more sensitive to fluoranthene than the sheepshead minnow. The numerical relationship between acute and chronic effects of fluoranthene on the mysid shrimp is small, with the chronic value being about one-half of the 96-hour LC50 value.

Acute Toxicity

The sheepshead minnow was exposed to concentrations of fluoranthene as high as 560,000 µg/l with no observed LC50 value (Table 7).

The unadjusted 96-hour LC50 value for the mysid shrimp is 40 µg/l (Table 4) and this result is used to derive the Final Invertebrate Acute Value of 0.69 µg/l which also becomes the Final Acute Value.

Chronic Toxicity

The chronic value for the mysid shrimp is 16 µg/l (Table 5) and when this concentration is divided by the species sensitivity factor (5.1) the Final Invertebrate Chronic Value of 3.1 µg/l is obtained. Since comparable data are not available for saltwater fish, 3.1 µg/l also is the Final Chronic Value. It is interesting to note that this Final Chronic Value, based on the mysid shrimp, is higher than the Final Acute Value , which was based on the same species.

This relationship can be explained by the small difference, discussed earlier, between the LC50 and chronic values and the fact that the acute sensitivity factor for invertebrate species (49) is about 10 times larger than that for chronic data (5.1).

Plant Effects

The 96-hour EC50 values for chlorophyll a and cell numbers of the alga, Skeletonema costatum, are 45,000 and 45,600 µg/l, respectively. The lower value becomes the Final Plant Value.

Residues

No measured steady-state bioconcentration factor (BCF) is available for fluoranthene. A BCF can be estimated using the calculated octanol-water partition coefficient of 79,000. This coefficient is used to derive an estimated BCF of 3,100 for aquatic organisms that contain about 8 percent lipids. If it is known that the diet of the wildlife of concern contains a significantly different lipid content, an appropriate adjustment in the estimated BCF should be made.

CRITERION FORMULATION

Saltwater - Aquatic Life

Summary of Available Data

The concentrations below have been rounded to two significant figures.

Final Fish Acute Value = not available

Final Invertebrate Acute Value = 0.69 µg/l

Final Acute Value = 0.69 µg/l

Final Fish Chronic Value = not available

Final Invertebrate Chronic Value = 3.1 µg/l

Final Plant Value = 45,000 µg/l

Residue Limited Toxicant Concentration = not available

Final Chronic Value = 3.1 µg/l

0.44 x Final Acute Value = 0.30 µg/l

The maximum concentration of fluoranthene is the Final Acute Value of 0.69 µg/l and the 24-hour average concentration is 0.44 times the Final Acute Value. No important adverse effects on saltwater organisms have been reported to be caused by concentrations lower than the 24-hour average concentration.

Criterion: For fluoranthene the criterion to protect saltwater aquatic life as derived using procedures other than the Guidelines is 0.30 µg/l as a 24-hour average and the concentration should not exceed 0.69 µg/l at any time.

Table 4. Marine invertebrate acute values for fluoranthene (U.S. EPA, 1978)

Organism	Bioassay Method*	Test Conc.**	Time (hrs)	LC50 (ug/l)	Adjusted LC50 (ug/l)
Mysid shrimp (juvenile), *Mysidopsis bahia*	S	U	96	40	33.9

* S = static
** U = unmeasured
Geometric mean of adjusted value = 33.9 µg/l $\frac{33.9}{49}$ = 0.69 µg/l

Table 5. Marine invertebrate chronic values for fluoranthene (U.S. EPA, 1978)

Organism	Test *	Limits (ug/l)	Chronic Value (ug/l)
Mysid shrimp, *Mysidopsis bahia*	LC	12- 22	16

* LC = life cycle or partial life cycle
Geometric mean of chronic value = 16 µg/l

$\frac{16}{5.1}$ = 3.1 µg/l

Lowest chronic value = 16 µg/l

Table 6. Marine plant effects for fluoranthene (U.S. EPA, 1978)

Organism	Effect	Concentration (ug/l)
Alga, *Skeletonema costatum*	EC50 96-hr chlorophyll *a*	45,000
Alga, *Skeletonema costatum*	EC50 96-hr cell numbers	45,600

Lowest plant value = 45,000 µg/l

Table 7. Other marine data for fluoranthene (U.S. EPA, 1978)

Organism	Test Duration	Effect	Result (ug/l)
Sheepshead minnow (adult), Cyprinodon variegatus	96 hrs	LC50	>560,000

Lowest value = >560,000 µg/l

REFERENCES

U.S. Environmental Protection AGency. 1978. In-depth studies on health and environmental impacts of selected water pollutants. U.S. Environ. Prot. AGency. Contract No. 68-01-4646.

EXPOSURE

Ingestion from Water

The sources of fluoranthene in water and its environment are both natural and man-made. The occurrence of fluoranthene in water sediments, bacteria, algae and plant materials in areas remote from industry and human habitation are suggestive of its natural origin. Suess (1970) has suggested that man-made sources of fluoranthene in surface waters arise from contamination of estuaries and coastal waters by shipping and harbor oil industrial and municipal effluents, atmospheric fallout, precipitation and road run-off.

The two most important properties influencing the levels of fluoranthene in water are its stability and solubility. Its relatively high molecular weight and relative non-polarity make fluoranthene very insoluble in water. Although the solubility of fluoranthene in water at 25° C is 265 µg/l (Klerens, 1950), its presence in environmental waters can be increased through micelle formation by optimum synthetic detergent concentrations and by the action of certain organic solvents.

Studies have shown that fluoranthene can be adsorbed and concentrated on a variety of particulate matter. Thus the presence of particulate matter in suspended and settled form in natural waters can be sources of relatively high concentrations of fluoranthene. Analyzing sediment samples from Buzzards Bay, Mass., Giger and Blumer (1974) determined the concentration of fluoranthene as 110 µg/kg to 790 µg/kg of dry sediment. Similarly, the analysis of recent sediments

from a Swiss lake and river showed the fluoranthene content as 0.42 µg/g and 0.39 µg/g of dry material respectively (Giger and Schaffner, 1978). The river particulate matter, on the other hand, was found to contain 5.7 µg/g of fluoranthene (Giger and Schaffner, 1978). The analysis of sediments from an English valley showed fluoranthene concentrations of 0.6 ug/g to 13.8 µg/g of dry sediments (John and Nickless, 1977). Similarly, there is evidence of accumulation of fluoranthene in edible aquatic organisms. Thus it is considered necessary to monitor fluoranthene levels not only in surface waters but also in contaminated water since the use of these waters for irrigation can also spread fluoranthene into other foodstuffs (Shabad and Il'nitskii, 1970).

Industrial effluents from oil refineries, coke production industries, gas works, plastic and dyestuff industries, and industries using high temperature furnaces are some of the primary sources of man-made fluoranthene (Harrison, et al. 1975). The fluoranthene level in an industrial effluent was determined to be 2198 ng/l (Borneff and Kunte, 1965). Except for pyrene, the level of fluoranthene from this industrial effluent was much higher than for all other individual polynuclear aromatic hydrocarbons (PAH's) determined.

The fluoranthene concentration in municipal effluents was determined by Borneff and Kunte (1965). The value in domestic effluents was determined to be 273 ng/l to 352 ng/l. Although fluoranthene can be found in human urine and feces, the levels found in domestic sewage are unlikely to originate exclusively and/or primarily from this source

(Harrison, et al. 1975). Other possible contributing sources include the washing of clothing, infiltration from soil, and washout from the atmosphere and road run-off (Harrison, et al. 1975). When the sewage contained a high percentage of industrial effluents, the fluoranthene level was found to be high and varied between 2660 ng/l to 3420 ng/l (Borneff and Kunte, 1965).

Road run-off can be an important factor in increasing the fluoranthene load in sewage. Fluoranthene in road run-off can arise in a number of ways. Bituminous road surfaces, (Borneff and Kunte, 1965) car tire wear (Falk, et al. 1964) and vehicle exhausts (McKee and McMahon, 1967; Commins, 1969) contribute to the increase of fluoranthene content in road run-off. Road run-off was primarily responsible for the increase of fluoranthene levels in sewage, from 352 ng/l on a dry day to 16,350 ng/l during a heavy rain (Borneff and Kunte, 1965). This finding of Borneff and Kunte has been confirmed by Acheson, et al. (1976) who found that highway run-off samples contained higher levels of fluoranthene (0.49 µg/l to 1.10 µg/l) than Thames river water (0.11 µg/l to 0.27 µg/l).

The removal of fluoranthene from water by conventional sewage treatment processes was investigated by Borneff and Kunte (1967). Removal of fluoranthene during primary sedimentation was found to be 62 percent to 66 percent (from an initial value of 3.23 µg/l - 43.5 µg/l to 1.22 µg/l - 14.6 µg/l) and the removal was 91 percent to 99 percent (final value of 0.28 - 0.26 µg/l) after biological purification with activated sludge processes.

The fluoranthene level in surface waters (lakes and rivers) was determined by a number of authors. Borneff and Kunte (1964, 1965) found the concentration of fluoranthene in German rivers to be in the range of 38.5 to 761 ng/l. Acheson, et al. (1975) determined the value of Thames river water in England as 140 to 360 ng/l. Analyzing fourteen water samples from the Winnipesaukee, Oyster and Cocheco rivers in New Hampshire, Keegan (1971) detected fluoranthene in three samples, and the concentration ranged from 320-1000 ng/l.

One surface water in England used for drinking water was analyzed for fluoranthene, and the concentration was found to be 150 ng/l (Harrison, et al. 1976). Surface waters in the U.S. were analyzed by Basu and Saxena (1977), Basu and Saxena (1978) and Basu, et al. (1978). These investigators detected fluoranthene in four of the seven waters sampled. The average fluoranthene concentration in the positive samples was 325.7 ng/l with a range of 23.5 ng/l to 408.3 ng/l. These authors also analyzed three ground water samples and failed to detect any fluoranthene.

The fluoranthene level in U.S. drinking waters were analyzed by Basu and Saxena (1977), Basu and Saxena (1978), and Basu, et al. (1978). Of the sixteen water supplies monitored, four showed positive fluoranthene levels. The concentrations of fluoranthene in the four positive samples were 2.4, 4.3, 8.9, and 94.5 ng/l, with an average of 27.5 ng/l. The analytical limit of detection for fluoranthene in these studies was 2.3 ng/l. The U.S. E.P.A. also conducted

the National Organic Monitoring Survey (NOMS, 1977) to determine the frequency of occurrence of fluoranthene in drinking water supplies. Seventeen out of 110 samples analyzed showed the presence of fluoranthene (limit of detection = 10 ng/l). The mean fluoranthene concentration in positive samples in this study was 20.0 ng/l, with a range of concentrations varying from 10 ng/l to 80 ng/l. The values for fluoranthene concentrations in various surface and drinking waters are shown in Table 1.

The removal of fluoranthene during drinking water treatment processes was studied by Harrison, et al. (1976). A fluoranthene concentration in river intake water of 150 ng/l was reduced to 140 ng/l when stored in a reservoir; reduced to 81 ng/l after filtration; and further reduced to 45 ng/l after chlorination. Thus there was a 70 percent total reduction of fluoranthene concentration. The removal efficiency with a full water treatment process involving fluocculation, activated carbon addition, filtration, and chlorination was studied by Basu and Saxena (1977), Basu and Saxena (1978), and Basu, et al. (1978). They found an 87.5 percent to 100 percent reduction in fluoranthene levels. The removal efficiency was 100 percent when two stages of activated carbon purification were used. These removal efficiencies are presented in Table 2.

There is no epidemiological evidence to prove that PAH's in general, and fluoranthene, in particullar, present in drinking water are related to the development of cancer (Andelman and Snodgrass, 1974). Also, Shabad and Il'nitskii (1970) stated that the amount of carcinogenic PAH's consumed

TABLE 1

Fluoranthene Concentrations in Various Water Samples

Water Source	Wastewater Containing: Domestic sewage (dry day)	Domestic sewage (heavy rain)	Domestic and industrial sewage	Surface water	Surface water used for drinking water	Ground Water	Drinking Water
Concentration (ng/l)	2 273-352	16350	3040 (2660-3420)[a]	320-1000 140-360 38.5-761	325.7 (23.5-408.3) 150	N.D.[b]	27.5 (2.4-94.5) 20.0 (10-80)
Reference	Borneff and Kunte, 1965	Borneff and Kunte, 1965	Borneff and Kunte, 1965	Keegan, 1971; Borneff and Kunte (1964, 1965); Acheson, et al. 1975	Basu and Saxena, 1977; Basu and Saxena, 1978 Basu, et al. 1978	Saxena and Basu, 1978	Basu and Saxena, 1977; Basu and Saxena, 1978 Basu, et al. 1978 NOMS, 1977

[a] Values in parentheses are concentration ranges

[b] N.D.: not detected

TABLE 2

Fluoranthene Removal Efficiencies as a Result of Water Treatment[a]

Water Source	Initial conc., ng/l	Final conc. ng/l	% Reduction
Pittsburg, Pa.	408.3	N.D.[b]	100
Huntington, Va.	23.5	2.4	89.7
Philadelphia, Pa.	114.3	8.9	92.2
Wheeling, W. Va.	756.5	94.5	87.5

[a]Ref. Basu and Saxena, 1977; Basu and Saxena, 1978; Basu, et al. 1978.
[b]N.D.: not detected.

by man in water is typically only 0.1 percent of the amount he consumes from food. Nevertheless, accumulation of PAH's in edible aquatic organisms can greatly increase this amount (Andelman and Snodgrass, 1974). The use of contaminated water for irrigation can also spread PAH's into other foodstuffs (Shabad and Il'nitskii, 1970). Therefore, in 1970 the World Health Organization (WHO, 1970) recommended that the concentration of six representative PAH's (including fluoranthene) in drinking water not exceed 0.2 µg/l. It further recommended that there should be at least one center in each country capable of carrying out investigations of PAH's in drinking water. However, from the data given for fluoranthene (Table 1) and the other PAH data available in the references provided, the PAH level in U.S. drinking waters is well below the W.H.O. recommended level.

Ingestion from Foods

PAH's formed through both natural and man-made sources can enter the food chain in a variety of ways. The absorption of PAH from the soil by various plant roots and translocation to the shoots is well documented (Lo and Sandi, 1978). Some plant waxes act as collectors of PAH present in polluted air (Hetteche, 1971). It has been shown that 10 percent of benzo(a)pyrene (BaP) in lettuce, kale, spinach, leeks, and tomatoes can be removed by cold water washing, an indication that it was originally deposited externally (Lo and Sandi, 1978). Oysters and clams collected from moderately polluted waters also concentrate PAH (Cahnmann and Kuratsune, 1957; Guerrero, et al. 1978). Food additives and food packing, and dairy waxes containing PAH's contribute to the enhancement of PAH levels in processed foods. Hexane, a commercial solvent used to extract edible vegetable oils is also a source of PAH contamination. PAH's present in food grade carbon blacks used for food processing can be transported to the food products. Curing smoke and other pyrolysis products used during food cooking add to the level of PAH's in food.

It has been demonstrated by Zitko (1975) that PAH's are not bioaccumulated along the food chain. However, Bjørseth (1978) concluded that both common and horse mussels bioaccumulated PAH's, although not to the same degree. Dunn and Stich (1976) have shown that mussels cannot metabolize BaP upon their removal from water. In water, mussels released 79 percent of naphthalene in three days, with a half-life

of 1.3 days. The BaP release from both clams and mussels in water took place with a half-life of 2-5 weeks.

The fluoranthene levels in various foods are discussed individually below.

Various European workers have reported the presence of PAH's in fruits and related products (IARC, 1973). However, fluoranthene concentrations were not reported in this IARC study. No study was reported from North America relating PAH levels in fruits and related products. Kuratsune and Hueper (1958, 1960) published PAH levels in coffee soot and roasted coffee. The coffee soot was found to contain 340-1000 ppb fluoranthene. The moderately dark and fully roasted (darkest) coffees contained 1 to 7 ppb and 0-15 ppb fluoranthene respectively. Grimmer and Hildebrandt (1967) determined the fluoranthene content in coconut and reported values of 0.3 ppb, 3.9 ppb and 92.7 ppb for fresh, sun-dried and smoke-dried coconut respectively. They concluded that smoke-dried copra had a higher fluoranthene content than either fresh or sun-dried copra.

Fluoranthene was also qualitatively detected from germinated rye, wheat, and lentil seedlings, although none was detected in the ungerminated products (Graf and Nowak, 1966). These authors also demonstrated the uptake of fluoranthene in radish from polluted environments. It should be mentioned here that according to Borneff (1977), the predominant human intake of PAH comes from fruits, vegetables and bread. He estimated that the PAH intake from these sources amounted to 3-4 mg per year.

The fluoranthene levels found in these products are shown in Table 3. The relatively high levels of fluoranthene found indicate that the heating of such oils might have led to a slight increase of fluoranthene concentration (Lo and Sandi, 1978). In a total diet study Howard, et al. (1968) found only trace amounts (less than 0.5 ppb) of seven PAH's (fluoranthene not studied) in the composite sample containing the fats, oils, and shortenings. However, Borneff (1977) estimated that the yearly human intake of PAH from these sources should be 0.1 mg.

Whereas raw meat does not normally contain fluoranthene, smoked or cooked meat may contain varying amounts of fluoranthene. The pyrolysis of fats, and incomplete combustion of the fuel contribute to the fluoranthene content in meats. Casing around the meat changes PAH levels in cooked meats. Cellulose casing is more effective as a barrier to the passage of PAH's than animal casing (Simon, et al. 1969). Further investigations have shown that the presence of PAH in broiled meats is directly proportional to the temperature of the treatment (Lijinsky and Ross, 1967). The dependency of fluoranthene content in meat and meat products on all the above factors, is summarized in Tables 4 and 5.

Fish from unpolluted waters usually do not contain detectable amounts of PAH. Smoked and cooked food, however, contain varying levels of fluoranthene. The amount of fluoranthene depends on the method of cooking, such as the nature of the heat source, temperature of combustion and degree of smoking in the case of smoked fish. In an FDA-sponsored

TABLE 3

Fluoranthene Levels in Vegetable Fats, Oils and Shortenings

Product	Concentration, ppb	Reference
Linseed oil (unrefined)	15.1	Grimmer & Hildebrandt, 1967
Cocoa butter oil (unrefined)	20.5	Grimmer & Hildebrandt, 1967
Coconut oil (smoke-dried)	372.0	Grimmer & Hildebrandt, 1967
Coconut oil (hot-air dried)	255.0	Biernoth & Rost, 1967
Coconut oil (commercial)	445.0	Biernoth & Rost, 1967
Coconut oil (dried copra and treated with slaked lime)	18.0	Biernoth & Rost, 1967
Cotton seed oil (unrefined)	7.0	Grimmer & Hildebrandt, 1967
Ground nut oil (unrefined)	8.4	Grimmer & Hildebrandt, 1967
Palm oil (unrefined)	7.1	Grimmer & Hildebrandt, 1967
Palm-kernel oil (unrefined)	39.0	Grimmer & Hildebrandt, 1967
Pumpkin seed oil	25.0	Biernoth & Rost, 1967
Rapeseed oil (unrefined)	10.9	Grimmer & Hildebrandt, 1967
Soyabean oil (unrefined)	6.4	Grimmer & Hildebrandt, 1967
Soyabean oil	1.3[a] (0.6-2.6)	Howard, et al. 1966
Sunflower oil	21.1	Grimmer & Hildebrandt, 1967
Wesson oil	N.D.[b]	Lijinsky & Shubik, 1965
n-paraffin oil (acid-washed for yeast fermentation)	1.9 (1.0-3.0)	McGinnis, 1975
n-paraffin oil (silica-gel treated for yeast fermentation)	3.8 (0.5-7.3)	McGinnis, 1975
Olive oil	3.2 (2.2-4.4)	Howard, et al. 1966
Peanut oil	3.3	Howard, et al. 1966

[a] Values in parenthesis are range in concentrations
[b] N.D.: not detected.

TABLE 4

Fluoranthene Levels in Meat and Meat Products
Under a Variety of Conditions

Product	Concentration, ppb	Reference
Charcoal broiled steak (lab. preparation)	20.0	Lijinsky & Shubik, 1965a
Charcoal broiled ribs (commercial)	49.0	Lijinsky & Shubik, 1965a
Charcoal broiled steak (commercial)	43.0	Lijinsky & Shubik, 1965a
Liquid smoke	10.0-16.0	Lijinsky & Shubik, 1965 & 1965
Smoked ham	14.0	Howard, et al. 1966a;
	0.6-2.9	Melanoski, et al. 1968;
	4-156	Lo & Sandi, 1978
Smoked bacon	8.0	Lijinsky & Shubik, 1965a
	35.0	Lo & Sandi, 1978
Smoked chipped beef	0.6	Howard, et al. 1966a
Smoked frankfurters	6.4	Howard, et al. 1966a
Smoked mutton (lab.)	4.6	Bailey & Dungal, 1958
Smoked mutton (commercial)	18.0	Thorsteinsson, 1969
Smoked pork roll	3.1	Howard, et al. 1966a
Smoked barbecued beef	2.0	Melanoski, et al. 1968
Smoked mutton sausage (commercial)	6.0	Thorsteinsson, 1969
Home-smoked mutton (close to store & with cover)	35.0	Thorsteinsson, 1969
Home-smoked mutton (close to store & with cover)	303.0	Thorsteinsson, 1969
Home-smoked mutton (distant from store & with cover)	47.0	Thorsteinsson, 1969
Home-smoked lamb	158.0	Thorsteinsson, 1969
Cold-smoked sausage (with casing)	40.0	Lo & Sandi, 1978
Cold-smoked sausage (without casing)	7.2	Lo & Sandi, 1978
Hot-smoked sausage (with casing)	35.2	Lo & Sandi, 1978
Hot-smoked sausage (without casing)	13.0	Lo & Sandi, 1978
Hot-smoked salami (without casing)	5.6	Lo & Sandi, 1978
Hot-smoked Mortadella (without casing)	22.0	Lo & Sandi, 1978

TABLE 5

Effect of Fat Content and Temperature of Cooking on Fluoranthene Levels in Cooked Meats (Lijinsky and Ross, 1967)

Product and Cooking Method	Concentration, ppb
Charcoal broiled:	
Hamburger, fat (hot)[a]	13.3
Hamburger, fat (cold)[a]	6.4
Hamburger, lean (hot)	0.3
Hamburger, lean (cold)	1.3
Hamburger (no drip pan)	0.2
Hamburger frozen (hot)	4.9
Pork Chop (hot)	22.5
Chicken (hot)	1.1
Sirloin Steak (hot)	12.6
T-bone Steak (hot)	19.8
Flame broiled:	
T-bone Steak (hot)	19.0

[a]cold: 25 cm. from heat source, hot: 7 cm from heat source, fat: 21% fat, lean: 7% fat

TABLE 6

Fluoranthene Levels in Fishes and Other Sea Foods

Product	Concentration, ppb	Reference
Unsmoked haddock	1.6	Howard, et al. 1966a
Unsmoked herring (salted)	0.8	Howard, et al. 1966a
Unsmoked salmon (canned)	1.8	Howard, et al. 1966a
Smoked Cod	0.5	Dungal, 1961
Smoked haddock	1.1	Lijinsky & Shubik, 1965a
Smoked herring	3.0	Howard, et al. 1966a
Smoked herring (dried)	1.8	Howard, et al. 1966a
Smoked Rod fish	4.0	Dungal, 1961
Smoked salmon	6.0	Lijinsky & Shubik, 1965
	3.2	Howard, et al. 1966a
Smoked sturgeon	2.4	Howard, et al. 1966a
Smoked trout	N.D.	Howard, et al. 1966a
	12.0	Thorsteinsson, 1969
Smoked white fish	4.6	Baily & Dungal, 1958
Smoked eel	4.0	Thorsteinsson, 1969
Smoked lump fish	2.0	Thorsteinsson, 1969
Horse mackeral (gas broiled)	3.6-7.0	Lo & Sandi, 1978
Horse mackeral (electric broiled)	0.2-5.2	Lo & Sandi; 1978
Kale	82-6760	Hetteche, 1971
Algae (Chlorella vulgaris)	650	Borneff, et al. 1968
Algae (Scenedermus acutus)	44	Payer, et al. 1975

study, PAH levels in unsmoked and smoked fish were compared (Howard, et al. 1966a, and 1966b).

In addition to fish, various other edible marine organisms were investigated and found to contain fluoranthene. The fluoranthene content in fish and other marine foods is presented in Table 6. According to a recent estimate by Borneff (1977), the total human intake of PAH from smoked meat, smoked fish and drinking water sources amounts to 0.05 mg per year.

A bioconcentration factor (BCF) relates the concentration of a chemical in water to the concentration in aquatic organisms, but BCF's are not available for the edible portions of all four major groups of aquatic organisms consumed in the United States. Since data indicate that the BCF for lipid-soluble compounds is proportional to percent lipids, BCF's can be adjusted to edible portions using data on percent lipids and the amounts of various species consumed by Americans. A recent survey on fish and shellfish consumption in the United States (Cordle et al., 1978) found that the per capita consumption is 18.7 g/day. From the data on the nineteen major species identified in the survey and data on the fat content of the edible portion of these species (Sidwell, et al., 1974), the relative consumption of the four major groups and the weighted average percent lipids for each group can be calculated:

Group	Consumption (Percent)	Weighted Average Percent Lipids
Freshwater fishes	12	4.8
Saltwater fishes	61	2.3
Saltwater molluscs	9	1.2
Saltwater decapods	18	1.2

Using the percentages for consumption and lipids for each of these groups, the weighted average percent lipids is 2.3 for consumed fish and shellfish.

No measured steady-state bioconcentration factor (BCF) is available for fluoranthene, but the equation "Log BCF = 0.76 Log P - 0.23" can be used (Veith et al., manuscript) to estimate the BCF for aquatic organisms that contain about eight percent lipids from the octanol-water partition coefficient of 79,000, the steady-state bioconcentration factor for fluoranthene is estimated to be 3,100. An adjustment factor of 2.3/8.0 = 0.2875 can be used to adjust the estimated BCF from the 8.0 percent lipids on which the equation is based to the 2.3 percent lipids that is the weighted average for consumed fish and shellfish. Thus, the weighted average bioconcentration factor for fluoranthene and the edible portion of all aquatic organisms consumed by Americans is calculated to be 3,100 x 0.2875 = 890.

The fluoranthene levels detected in a variety of dairy and bakery products are listed in Table 7.

TABLE 7

Fluoranthene Concentrations Determined in Various Dairy and Bakery Products

Product	Baking Yeast				Browning Yeast	Smoked gouda cheese	Cheddar cheese
	French	German	Scottish	Russian			
Concentration, ppb	18.5-21.2	17.2-66.8	93.5	32.1	8.6	2.8	0.8
Reference	Grimmer, 1974				Grimmer, 1974	Howard, et al. 1966a	Howard, et al. 1966a

Inhalation

A variety of PAH's including fluoranthene have been detected in ambient air. Because of its carcinogenic properties, BaP has been most extensively monitored and has frequently been used as an indicator of ambient PAH's. However, the relative amount of individual PAH's in ambient air is dependent on the source. This has been demonstrated by Stocks, et al. (1961) by studying ambient rural, suburban and urban air in England. The exact amount of fluoranthene intake as a result of inhalation is difficult to determine because of the different sources of exposure, such as, tobacco smoke inhalation, occupational exposure, and exposure to ambient air. The fluoranthene exposure due only to inhalation of ambient air will be discussed in this section.

Concentrations of fluoranthene are different in various cities and at different times of the year. In general, the concentrations are usually highest during the winter months in areas using heat during this period. Probably, the increase in fluoranthene concentration in winter is due to the contribution of fluoranthene from heating sources (Sawicki, 1962). However, there may be some exceptions to this high winter-low summer concentration pattern. It has been suggested that in areas with significant industrial emissions of PAH's the fluoranthene level may remain uniform throughout the year (U.S. E.P.A., 1974). In other areas such as Los Angeles, which do not require heating during winter, automobile and industrial emissions control the PAH pattern in the ambient air (Gordon, 1976). The fluoranthene concentration in Los Angeles ambient air during the four quarterly periods May-July, Aug.-Oct., Nov.-Jan., and Feb.-Apr. were 0.38 ppb, 0.15 ppb, 0.24 ppb, and 0.68 ppb respectively (Gordon, 1976).

The declining trend of fluoranthene concentration in U.S. ambient air from the 1960's to 1970's may be due to the decline in the use of coal for power generation. Also contributing to this decline is the improved disposal of solid wastes and restrictions on open burning (U.S. E.P.A., 1974).

The possibility of long distance transport of PAH's which might result in PAH contamination in areas that are downwind from large emission sources has been studied by Lunde and Bjørseth (1977). They determined that samples with trajectories from Western Europe contained about 20 times more fluoranthene than samples with trajectories from Northern Norway. This proves that some PAH's including fluoranthene are stable enough to be transported from far away industrial sources to the suburban and rural areas.

The fluoranthene levels determined in various locations and at different times are presented in Table 8.

Various factors, particularly smoking, can alter the concentration of fluoranthene in indoor environments. Under standard smoking conditions the smoke of a cigarette generated between puffs (sidestream-smoke) contains 1,255 ng of fluoranthene per cigarette compared to the smoke which is inhaled (mainstream-smoke) which contains 272 ng of fluoranthene per cigarette (Grimmer, et al. 1977). In a 36 m^3 room with ventilation equal to a single air change per hour, the smoke from 5 cigarettes per hour from 2 smokers produced an average level of 99 ng/m^3 of fluoranthene in air samples collected over a period of 8 hours from an average of two tests (Grimmer, et al. 1977).

TABLE 8

Ambient Fluoranthene Levels at Different Locations

Location	Concentration, μg/1000m^3	Reference
Average U.S. Urban air, 1963[a]	4.0	Hoffman & Wynder, 1968
Birmingham, Alabama, 1964-65	5.5	U.S.E.P.A. 1975
Detroit, 1965	0.19-15.0	Hoffman & Wynder, 1968
Los Angeles, 1973	0.1-3.4	Hoffman & Wynder, 1977
College Park, Md., 1976	4.1	Fox & Staley, 1976
Baltimore Harbor Tunnel, 1976	93.0	Fox & Staley, 1976
Los Angeles, 1976	0.31	Gordon, 1976
Providence, R.I., 1977	0.16-1.5	Krstulovic, et al. 1977
England, Urban, 1961		
Summer	6.5	Stocks, et al. 1961
Winter	44.9	
England, Bus Depot, 1961		
Summer	5.0	Stocks, et al. 1961
Winter	40.0	
England, us Garage, 1961		
Summer	5.0	
Winter	83.0	Stocks, et al. 1961
England Tunnel, 1961		
Summer	24.0	Stocks, et al. 1961
Winter	54.5	
England Suburban, 1961		
Summer	4.6	Stocks, et al. 1961
Winter	26.6	
England, Rural, 1961		
Summer	4.5	Stocks, et al. 1961
Winter	10.5	
Rome, 1966	2.1-4.5	Hoffman & Wynder, 1977
Rome, 1972	1.0-18.0	Hoffman & Wynder, 1977
Rome, 1975		
Summer	3.1	Liberti, et al. 1976
Winter	8.4	
Budapest, 1975	10.4	Kertesz-Saringer & Morlin, 1975
Sidney, 1965	0.06-2.6	Hoffman & Wynder, 1977
Ontario, 1966	0.3-10.6	Hoffman & Wynder, 1977
Ontario, 1962 inversion period	0.6-41.0	Hoffman & Wynder, 1977
Norway, 1977	0.17-0.32	Lunde & Bjørseth, 1977
Switzerland, 1978	12.9	Giger & Schaffner, 1978
Ohmuta, Japan, 1978	5.75	Tokiwa, et al. 1977

Dermal

No direct information is available on the importance of dermal absorption in total human exposure to fluoranthene. Fluoranthene can be absorbed across the skin by animals (see Absorption section). For those humans exposed to only background levels of fluoranthene, dermal absorption is not likely to be a significant route of entry.

PHARMACOKINETICS

There are no data available concerning the pharmacokinetics of fluoranthene or other PAH's in humans. Moreover, animal studies have not been conducted for the specific purpose of supplying pharmacokinetic data on fluoranthene. Nevertheless, it is possible to make limited assumptions based on the results of animals studies conducted with other PAH's which are structurally similar to fluoranthene.

Absorption

The demonstrated toxicity of fluoranthene by oral and dermal administration (Smyth, et al. 1962) indicates that it is capable of passage across epithelial membranes. The high lipid solubility of fluoranthene supports this observation. Animals studies with structurally-related PAH's such as benzo(a)pyrene, chrysene, 7, 12-dimethylbenz(a)anthracene, benz(a)anthracene, and 3-methylcholanthrene confirmed that intestinal transport readily occurs, primarily by passive diffusion (Ress, et al. 1971). In addition, there is ample evidence to indicate that benzo(a)pyrene (and presumably other PAH's) is easilly adsorbed through the lungs (Kotin, et al. 1959; Vainio, et al. 1976).

Distribution

The tissue distribution and accumulation of fluoranthene has not been studied. It is known, however, that other PAH's (e.g., benzo(a)pyrene, 7, 12-dimethylbenz(a)anthracene, 3-methylcholanthrene, phenanthrene) become localized in a wide variety of body tissues following their absorption in experimental rodents (Kotin, et al. 1959; Bock and Dao, 1961; Dao, et al. 1959; Flesher, 1967). Relative to other tissues, PAH's such as fluoranthene can be expected to localize primarily in body fat and fatty tissues.

The potential for transplacental passage of fluoranthene cannot be predicted. With other PAH's, passage into the fetus following intragastric or intravenous administration to pregnant rats has been variable (Shendrikova and Aleksandrov, 1974).

Metabolism

Experimental studies have not been conducted on the metabolism of fluoranthene. However, it is well-established that the metabolism of PAH's is accomplished by the microsomal enzyme complex of mixed-function oxidases, often termed aryl hydrocarbon hydroxylase. This enzyme system has been studied extensively and is the subject of numerous reviews (Conney, 1967; Gelgoin, 1967; Marquardt, 1976). These microsomal oxidases, while most abundant in the liver, have been found in most mammalian tissues. It is this enzyme complex which is responsible for the metabolic detoxification of PAH's, but also has the capability for activation of PAH's to toxic and carcinogenic metabolites.

As a group, PAH's are metabolized to substances that have been arbitrarily divided into two groups on the basis of solubility. In one group are those metabolites which can be extracted from an aqueous incubation mixture by an organic solvent. This group consists of ring-hydroxylated products such as phenols and dihydrodiols. Numerous studies indicate that epoxide intermediates are involved in the formation of phenolic metabolites, and are critical for the expression of toxic and carcinogenic effects (Sims and Grover, 1974; Sims, 1976; Jerina and Daly, 1974; Jerina, et al. 1977).

In the second group of metabolites are water-soluble products that remain after extraction with an organic solvent. It is generally agreed that most of these PAH derivatives are formed by conjugation of the hydroxylated products to glutathione or glucuronic acid and sulfate. This process would render the derivatives more hydrophilic and presumably less toxic.

It is reasonable to assume that fluoranthene is metabolized in a manner which is consistent with the general biochemical scheme for biotransformation of PAH's. However, the exact chemical structure of fluoranthene metabolites or their chemical and biological reactivity is not presently known.

Excretion

There is no direct information available concerning the excretion of fluoranthene in experimental animals or man. Limited inferences can be drawn from animal studies with related PAH's, however.

As long ago as 1936, it was recognized that various PAH's were excreted primarily through the hepatobiliary system and the feces (Peacock, 1936; Chalmers and Kirby, 1940). However, the rate of disappearance of various PAH's from the body, and the principal routes of excretion are influenced both by structure of the parent compound and the route of administration (Heidelberger and Weiss, 1951; Aitio, 1974). Moreover, it has been shown that the rate of disappearance of a PAH (i.e. benzo(a)pyrene) from body tissues can be markedly stimulated by prior treatment with inducers of microsomal enzymes (e.g., benzo(a)pyrene, 7, 12-dimethylbenz(a)anthracene, 3-methylcholanthrene, chrysene) (Schlede, et al. 1970a, 1970b; Welch, et al. 1972). From the available evidence concerning excretion of PAH's in animals, it is apparent that extensive bioaccumulation is not likely to occur.

EFFECTS

Acute, Subacute, and Chronic Toxicity

Smyth and coworkers (1962) determined the acute toxicity of fluoranthene following oral and inhalation exposures in rats, and dermal administration to rabbits. The acute oral LD_{50} for fluoranthene, determined using groups of five male Carworth-Wistar rats, was 2.00 g/kg body weight (range 1.27 to 3.13 g/kg). The dermal LD_{50} in rabbits resulting from 24 hour contact with fluoranthene was 3.18 g/kg body weight (range 2.35 to 4.29 g/kg). Exposure of six male or female albino rats to concentrated vapors of fluoranthene for eight hours produced no mortality. Taken together,

these results from animal studies indicate that fluoranthene presents a relatively low degree of toxic potential from acute exposure. Where deaths occurred, no information was reported concerning target organs or specific cause of death.

In earlier studies, Haddow and coworkers (1937) examined the effect of various PAH's including fluoranthene, on body growth in hooded rats of the Lister strain. A single intraperitoneal injection of 30 mg fluoranthene dissolved in sesame oil had no adverse effect on body weight gain over a 24 day observation period. By comparison, certain carcinogenic PAH's (10 mg. benzo(a)pyrene or dibenz(a,h)anthracene) caused an initial weight reduction followed by resumption of growth at a reduced rate.

Only limited data are available concerning the toxic effects of fluoranthene produced by repeated administration. These are limited to reports of mortality produced in mice by repeated dermal application or subcutaneous injection. Pertinent data from these studies are summarized in Table 9.

Synergism and/or Antagonism

Because fluoranthene is normally encountered in the environment as part of a complex mixture of PAH's, concern has often been expressed over its interactive toxic effects. In this regard, Pfeiffer (1973, 1977) tested ten non-carcinogenic PAH's found in automobile exhaust in combination with benzo(a)pyrene (3-100 µg) and dibenz(a,h)anthracene (2-75 µg) by subcutaneous injection in groups of female NMRI mice. The ten non-carcinogens tested were: benzo(e)pyrene (2-70 µg); benz(a)anthracene (3-100 µg); phenanthrene (125-4000

TABLE 9

Toxicity of Fluoranthene by Repeated Administration to Mice

Species	No.	Sex	Preparation and Dose	Route of Administration	Effect	Reference
Mouse (Strain A)	14	M&F	10 mg crystalline fluoranthene in glycerol, repeated 4 times	subcutaneous injection in the left flank	6 mice survived for 18 months; experiment terminated at 19 months	Shear, 1938
Mouse	10	?	0.3 % solution of fluoranthene in benzene applied twice weekly	dermal application to interscapular region	3 of 10 alive after 6 months; 3 of 10 alive after 1 year; last mouse died after 501 days	Barry, et al 1935
Mouse	10	?	0.3 % solution of fluoranthene in benzene applied twice weekly	dermal application to interscapular region	4 of 10 alive after 6 months; 1 of 10 alive after 1 year; last mouse died after 379 days	Barry, et al 1935
Mouse (Ha/ICR/Mil Swiss Albino	20	F	50 µl of 1.0% fluoranthene solution in acetone applied 3 times weekly for 12 months	dermal application	No mortality after 15 months	Hoffman, et al. 1972

μg); anthracene (31-1000 μg); pyrene (62-2100 μg); chrysene (3-100 μg); perylene (0.2-7.0 μg); benzo(g,h,i)perylene (12.8 - 410 μg); coroene (3-100 μg); and fluoranthene (28-900 μg). The tumor incidence resulting from all 12 compounds being administered together could be attributed to the presence of dibenz(a,h)anthracent, with little influence from benzo(a)-pyrene or the other ten chemicals. No inhibitory effect of the ten non-carcinogens was evident; moreover, an increased tumor yield resulted from injection of mixtures containing increasing amounts of the components. This effect, however, was less dramatic than if benzo(a)pyrene were administered alone, and paralleled the dose-response curve of dibenz(a,h)-anthracene acting singularly.

Similar experiments were conducted by Schmal and coworkers (1977) involving the dermal application of mixtures containing carcinogenic and nocarcinogenic PAH's to mice. They concluded that the tumorigenic response obtained with PAH mixtures which included fluoranthene could be attributed almost entirely to the presence of the carcinogenic PAH's (benzo(a)pyrene, dibenz(a,h)anthracene, benz(a)anthracene, benzo(b)fluoranthene) in the mixture.

Evidence is available, however, which indicates that fluoranthene may considerably enhance the tumorigenic response produced by benzo(a)pyrene. These studies are discussed in the Carcinogenicity section of this report.

Teratogenicity

There is no information available concerning the possible teratogenic effects of fluoranthene in animals or man. Furthermore, only limited data are available regarding the teratogenic effects of other PAH's in experimental animals.

Benzo(a)pyrene had little effect on fertility or the developing embryo in several mammalian and non-mammalian species (Rigdon and Rennels, 1964; Rigdon and Neal, 1965). On the other hand, 7, 12-dimethylbenz(a)anthracene and its hydroxzymethyl derivatives apparently possess considerable teratogenic potency in the rat (Currie, et al. 1970; Bird, et al. 1970).

Mutagenicity

The concept that carcinogenesis is an expression of an alteration in the genetic material of a cell (i.e., somatic mutation) implies that a formal relationship exists between mutagenesis and carcinogenesis (Nery, 1976; Miller, 1978). The results obtained with several in vitro mutagenesis test systems, particularly the Ames Salmonella typhimurium assay, support the belief that most carcinogenic chemicals are mutagenic as well. For PAH's, the Ames assay has been very effective in detecting parent structures and their biotransformation products which possess carcinogenic activity (McCann, et al. 1973; Teranishi, et al. 1975; McCann and Ames, 1976; Sugimura, et al. 1976; Wislocki, et al. 1976; Wood, et al. 1976).

Tokiwa and coworkers (1977) employed the Ames assay to search for mutagenic activity in a series of PAH's, including fluoranthene, which were detected in the particulate fraction of urban air pollutants. Salmonella strain TA 98 in the presence of rat liver S-9 fraction (to provide bioactivation) was employed. Under these test conditions, fluoranthene displayed no mutagenic activity.

In a comparative study of the mutagenic activity, tumor initiating activity, and complete carcinogenicity of several PAH, fluoranthene was also found to be inactive towards both tester strains TA 98 and TA 100 in the presence of Araclor 1254 induced rat liver homogenate (LaVoie, et al. 1978).

No reports are available regarding the potential mutagenicity of fluoranthene in other test systems, either *in vitro* or *in vivo*.

Carcinogenicity

Among the unsubstituted polycyclic hydrocarbons containing a non-aromatic rings, a number of active carcinogens are known. The most prominent examples of this type of compound are: cholanthrene; 11, 12-ace-benz(a)anthracene; 6, 7-ace-benz(a)anthracene; 8, 9-cyclopentabenz(a)anthracene; acenaphthanthracene; 1,2,5,6-tetrahydrobenzo(j)cyclopenta(f,g)aceanthrylene, and "angular" stearanthrene (Arcos and Argus, 1974). In addition, alkyl substitution of partially and fully aromatic condensed ring systems may also add considerable carcinogenic activity. The best examples of this type of activation are 3-methylcholanthrene, a highly potent carcinogen, 2-methyl-fluoranthene and 5-methylchrysene.

Fluoranthene was first tested for carcinogenic activity more than four decades ago (Barry, et al. 1935). The results from that investigation, and from several studies conducted since that time, indicate that fluoranthene has virtually no activity as a complete carcinogen. The conditions employed and results obtained in these studies are summarized in

Table 10. Both dermal application and subcutaneous injection in mice have been employed for the bioassay of fluoranthene.

Despite the fact that fluoranthene shows no activity as a complete carcinogen in the mouse, a number of fluoranthene derivatives are active carcinogens. These include 2-methylfluoranthene (Hoffmann, et al. 1972), and several benzofluoranthenes and dibenzofluoranthenes (IARC, 1973; Arcos and Argus, 1974).

From investigations in which polycyclic carcinogens were applied to the skin of mice has emerged the two-stage theory of skin carcinogenesis (Van Duuren, 1969, 1976). The first stage, initiation, results from the ability of a carcinogen to effect a permanent change within a cell or cell population following a single application. The measure of carcinogenic potency is often regarded as the capacity for tumor initiation. However, some weak or inactive complete carcinogens can be active as tumor initiators (e.g., dibenz(a,c)anthracene, 1-methylchrysene, benz(a)anthracene). The second stage, promotion, is a prolonged process which does not necessarily require the presence of a carcinogen, but nevertheless a chemical stimulus must be supplied (e.g., by croton oil). A complete carcinogen is one which is capable of producing tumors when applied alone in sufficient quantity.

It has been established for many years that fluoranthene is inactive as a complete carcinogen. In recent years fluoranthene has also been tested for tumor initiating and promoting activity (Hoffmann, et al. 1972; Van Duuren and Goldschmidt, 1976).

TABLE 10

Activity of Fluoranthene as a Complete Carcinogen in Mice

Species	No.	Sex	Preparation and Dose	Route of Administration	Results	Reference
Mouse	10	?	0.3% solution of fluoranthene in benzene, applied twice weekly	dermal application to interscapular region	70% mortality after 6 months; no tumors by 1 year	Barry, et al. 1935
Mouse	10	?	0.3% solution of fluoranthene in benzene, applied twice weekly	dermal application to interscapular region	60% mortality after 6 months; no tumors by 1 year	Barry, et al. 1935
Mouse (Strain A)	14	M&F	10 mg. crystalline fluoranthene in glycerol, repeated 4 times	subcutaneous injection in the left flank	6 mice survived for 18 months; no tumors by 19 months	Shear, 1938
Mouse (CAF, Jackson)	25-50	M&F	10% solution of fluoranthene in acetone 3 times weekly	dermal application to the back	No papillomas or carcinomas found by 13 months	Suntzeff, et al. 1957
Mouse (Swiss, Millerton	25-50	M&F	10% solution of fluoranthene in acetone applied 3 times weekly	dermal application to the back	No papillomas or carcinomas found by 13 months	Suntzeff, et al. 1957
Mouse	20	M&F	not specified	subcutaneous injection	No sarcomas produced	Buu-hoi, 1964

Mouse (Ha/ICR/Mil Swiss Albino)	20	F	50 µl of 1.0% fluoranthene solution in acetone applied 3 times weekly for 12 months	dermal application	No tumors observed after 15 months; no mortality encountered	Hoffmann, et al. 1972
Mouse (C3H)	15	M	50 mg fluoranthene as an 0.5% solution in Decalin applied 2 times each week for 82 weeks	dermal application	No skin tumors observed; 13 of 15 mice were alive at 52 weeks	Horton and Christian, 197
Mouse (C3H)	15	M	50 mg fluoranthene as an 0.5% solution in 50:50 Decalin-n-dodecane applied 2 times each week for 82 weeks	dermal application	No skin tumors observed; 12 of 15 mice were alive at 52 weeks	Horton and Christian, 197
Mouse (ICR/Ha Swiss)	50	F	40 µg flouranthene in acetone applied 3 times weekly for 440 days	dermal application	No skin tumors observed	Van Duuren and Goldschmidt, 1976

Fluoranthene was applied repeatedly to the shaved backs of mice and followed by application of croton oil (a known tumor promoter) to test for initiating activity (Hoffmann, et al. 1972). As indicated in Table 11, fluoranthene displayed no significant capacity for tumor initiation.

TABLE 11

Tumor Initiating Activity of Fluoranthene[a]
(data from Hoffmann, et al. 1972)

Species	No.	Sex	Dose and Preparation	Tumors After 20 weeks
Mouse (Swiss-Albino Ha/ICR/Mill)	30	F	0.1 mg fluoranthene in 50 µl acetone applied every 2nd day for 10 applications	1[b](1)[c]29[d]
Mouse	30	F	10 x 5 µg benzo(a)-pyrene[e]	19(67)29

[a]Ten days after last application of fluoranthene, the tumor promoter 2.5% croton oil in acetone, average dose 3.8 mg, was applied for 20 weeks
[b]Tumor-bearing mice
[c]Number in parenthesis = total number of tumors
[d]Surviving mice
[e]Positive control

In related studies conducted by Van Duuren and Goldschmidt (1976) fluoranthene was tested as a tumor promoter in a two-stage carcinogenesis test system. Their results were equivocal and indicated that, at best, fluoranthene was only a very weak tumor promoter in comparison to the action of classical tumor promoting chemicals such as phorbol myristate acetate (the active component of croton oil) (Table 12).

TABLE 12

Two-stage Carcinogenesis: Tumor-Promoting Activity of Cocarcinogens and Inactive Analogues[a]
(Van Duuren and Goldschmidt, 1976)

Secondary[b] treatment (dose)	Days of testing	Median Survival time, days	Days to first papilloma	Mice with papillomas/total Papillomas[c]
Pyrene (40 µg)	448	<448	414	1/1 (1)
Fluoranthene (40 µg)	448	<448	401	1/1 (1)
Catechol (2 mg)	448	<448	---	0
Resorcinol (10 mg)	449	<449	---	0
Hydroquinone (5 mg)	409	<409	---	0
Pyrogallol (5 mg)	449	<449	328	1/1 (0)
PMA (2.5 µg)	449	357	54	43/155 (18)
Anthralin (80 µg)	434	<434	85	9/14 (2)
Acetone	450	<450	---	0
No treatment[d]	443	<427	---	0
PMA alone (2.5 µg)	368	?	174	5/5 (0)

[a]We used 50 female ICR/Ha Swiss mice per group, except for the anthralin experiment with which 20 mice were used.

[b]150 µg B(a)P/0.1 ml acetone applied to dorsal skin once by micropipette. For the anthralin experiment, the initiating dose was 100 µg B(a)P. For the duration of the test, the promoters were applied to the dorsal skin 3 times weekly in 0.1 ml acetone beginning 14 days after initiator. For data on the application of promoting compounds, see Table 2.

[c]Numbers in parentheses are numbers of mice with squamous carcinoma.

[d]100 mice.

The most remarkable aspect of the biological activity of fluoranthene concerns its potential to act as a potent cocarcinogen. The designation of a cocarcinogen is here intended to denote a compound which, upon repeated application to mouse skin together with low doses of a complete carcinogen such as benzo(a)pyrene, produces a considerable enhancement in carcinogenic effect (Van Duuren, 1976). It should be noted that, by this definition, a cocarcinogen need not necessarily possess either tumor initiating or tumor promoting activity in the two-stage carcinogenesis system.

It was first recognized by Hoffmann and Wynder (1963) in studies on the components of gasoline engine exhaust that fluoranthene could enhance the yield of benzo(a)pyrene-induced skin carcinomas in mice. These results are depicted in Figures 1 and 2. Although the details of their experimental protocol were not reported, the authors concluded that the potential interaction of components in complex environmental mixtures dictates the need for caution in interpretation of results. In particular, the extrapolation of results from animal bioassays with single chemicals may not provide a realistic estimate of human risk resulting from exposure to these chemicals in combination.

A more detailed investigation of the cocarcinogenic activity of fluoranthene was undertaken by Van Duuren and Goldschmidt (1976). In their study, fluoranthene not only increased the total number of papillomas and carcinomas produced by benzo(a)pyrene on mouse skin, but also decreased the days to the appearance of the first tumor as compared

Effect of Fluoranthene on Production of Skin Carcinomas in Mice
(Hoffmann and Wynder, 1963)

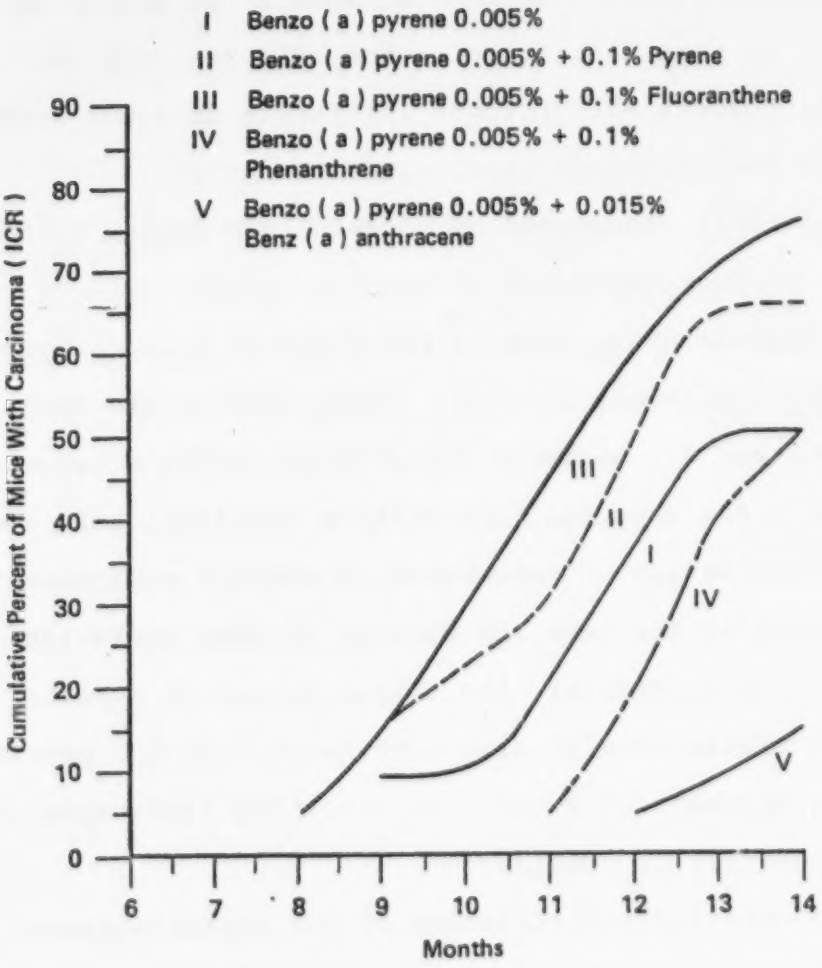

Figure 1

Effect of Fluoranthene on Production of Skin Tumors in Mice
(Hoffmann and Wynder, 1963)

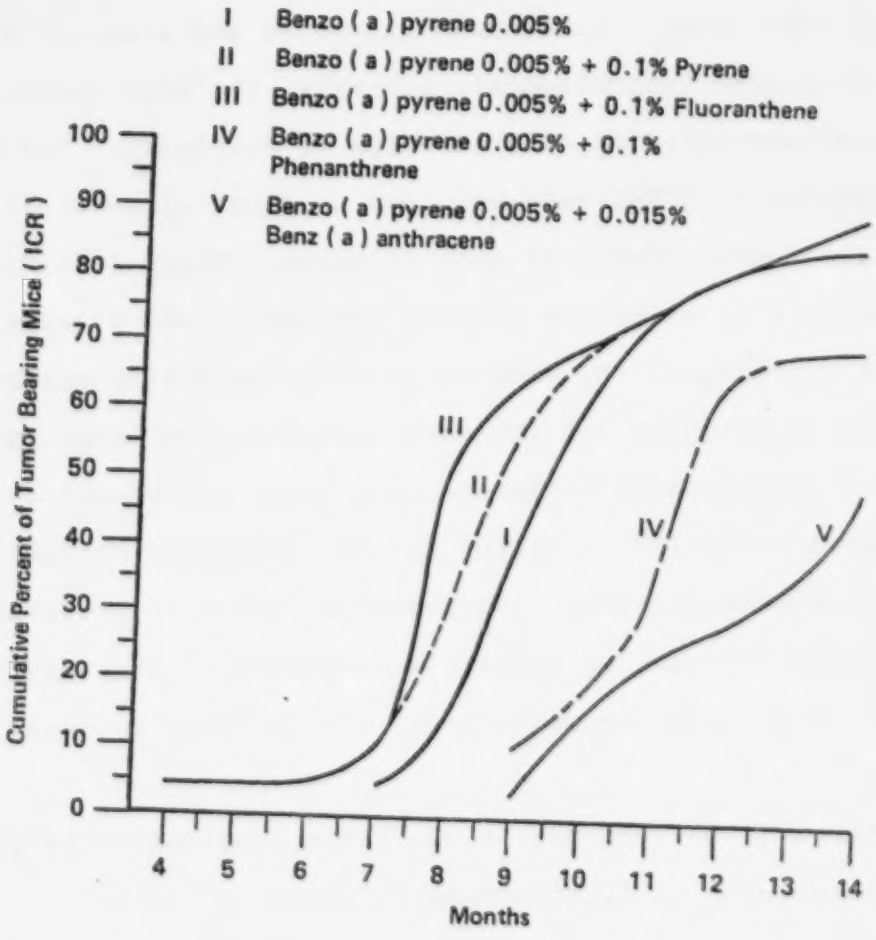

Figure 2

to mice treated with benzo(a)pyrene only (Table 13). Among all the cocarcinogens tested in this study, only fluoranthene caused a marked decrease in the tumor latency period. These results led the authors to conclude that fluoranthene possesses potent cocarcinogenic activity.

The mechanism of action for cocarcinogenic compounds is not understood. Since both aliphatic and aromatic compounds have displayed cocarcinogenic activity, the elucidation of structure-activity relationships is difficult. Van Duuren and coworkers (1978) have proposed a number of possibilities to explain the effects of cocarcinogens. These include: (a) ability to alter the rate of absorption and disappearance of the carcinogen; (b) ability to alter metabolic pathways for the carcinogen; and (c) metal-chelating ability. However, none of these possibilities is considered acceptable as a general mechanism of action for all compounds displaying cocarcinogenic activity. Furthermore, there is presently not enough information available to determine the importance of the cocarcinogenic activity of fluoranthene to human health.

There is no information available concerning the potential carcinogenicity of fluoranthene to humans.

TABLE 13

Cocarcinogenesis: Bioassay in Mouse Skin
(Data from Van Duuren and Goldschmidt, 1976)[a]

Carcinogen[b]	Cocarcinogen (dose)	Days on test	Days to first Papilloma	Mice with Papillomas/total Papillomas[c]
Benzo(a)pyrene	Fluoranthene (40µg)	440	99	39/126 (37)
none	Fluoranthene (40µg)	440	___	0
Benzo(a)pyrene	Acetone	440	210	16/26 (12)
none	Acetone	440	___	0
none	none[d]	440	___	0

[a]50 female ICR/Ha Swiss mice used per group.

[b]Benzo(a)pyrene was applied in the same solution as the cocarcinogen (5 µg/0.1 ml acetone) three times weekly to the dorsal skin.

[c]Numbers in parentheses are numbers of mice with squamous carcinoma

[d]100 animals

CRITERION RATIONALE

Existing Guidelines and Standards

There have been no standards developed for fluoranthene in air, water, and food, or in the workplace. The only existing standard which takes fluoranthene into consideration is a drinking water standard for PAH's. The 1970 World Health Organization European Standards for Drinking Water recommends a concentration of PAH's not exceeding 0.2 ug/l. This recommended standard is based upon the analysis of six PAH's in drinking water:

Fluoranthene
Benzo(a)pyrene
Benzo(g,h,i)perylene
Benzo(b)fluoranthene
Benzo(k)fluoranthene
Indeno(1,2,3-cd)pyrene

The designation of the above six PAH's for analytical monitoring of drinking water was not made on the basis of potential health effects or bioassay data on these compounds (Borneff and Kunte, 1969). Thus it should not be assumed that these six compounds have special significance in determining the likelihood of adverse health effects resulting from absorption of any particular PAH. They are, instead, considered to be a useful indicator for the presence of PAH pollutants. Borneff and Kunte (1969) found that PAH's were present in ground water at concentrations up to 50 ng/l, and in drinking water at concentrations up to 100 ng/l. Based on these data they suggested that water containing more than 200 ng/l should be rejected. However, as data from a number of U.S. cities indicate (see Ingestion from Water section), levels of PAH's in raw and finished waters are typically much less than the 0.2 ug/l criterion.

Current Levels of Exposure

Quantitative estimates of human exposure to fluoranthene require numerous assumptions concerning routes of exposure, extent of absorption, conformity of lifestyle, and lack of geographic-, sex-, and age-specific variables. Nevertheless, working with estimates developed for PAH as a class, certain extrapolations are possible to arrive at an admittedly crude estimate of fluoranthene exposure.

An estimate of fluoranthene intake from drinking water may be derived from data obtained in a survey of 16 U.S. cities (Basu and Saxena, 1978; Basu and Saxena, 1977-78). By arbitrarily assigning the lower limit of detectability for fluoranthene to those samples where none was detected, and using the measured values of fluoranthene in the four positive samples found, the estimated average fluoranthene level in drinking water would be 8.6 ng/l. Thus the daily intake of fluoranthene in drinking water may be calculated:

8.6 ng/l x 2 liters/day = 17.2 ng/day

Borneff (1977) estimates that the daily dietary intake of PAH's is about 8-11 µg/day. As a check on this estimate, fluoranthene intake may be calculated bases on reported concentrations of fluoranthene in various foods (see Distribution section of the document) and the per capita estimates of food consumption by the International Commission on Radiological Protection (1974). Taking a range of 1-10 ppb as a typical concentration for fluoranthene in various foods, and 1600 g/day as the total daily food consumption by man from all types of foods (i.e. fruits, vegetables, cereals, dairy products, etc.), the intake of fluoranthene from the diet would be in the range of 1.6-16 µg/day.

It has recently been reported that fluoranthene concentrations in ambient air average about 4 μg/1000 m^3 (Santodonato, et al. 1978). If it is assumed that 100 percent of the fluoranthene which is inhaled is adsorbed, and that the average amount of air inhaled by a human each day is about 10-20 m^3, then fluoranthene intake via the air would be in the range of 40-80 ng/day. However, in certain indoor environments, particularly in the presence of sidestream tobacco smoke, PAH exposure from inhaled air may be considerably higher (Grimmer, et al. 1977).

In summary, a crude estimate of total daily exposure to fluoranthene would be as follows:

Source	Estimated Exposure
Water	0.017 μg/day
Food	1.6 - 16 μg/day
Air	0.040 - 0.080 μg/day

The figures presented above make it quite clear that foods are by far the greatest source of fluoranthene to humans. The present levels of fluoranthene in drinking water would be expected to contribute very little to the total human intake.

It is important to note two factors which are not taken into account in the above estimate. First, it is known that tobacco smoking can contribute greatly to fluoranthene exposure in man. It is estimated that smoking one cigarette will increase exposure to fluoranthene via the lungs by about 0.26 μg (Hoffmann, et al. 1972). The sum of methyl-fluor-anthenes in the smoke of a non-filtered cigarette is about 0.18 ng (Hoffmann, et al. 1972). Second, it is

assumed that the possibility of dermal absorption for fluoranthene contributes only a negligible amount to the total exposure. It is expected that only in certain occupational situations would dermal exposure be a quantitatively important route of exposure.

Special Groups at Risk

Individuals living in areas which are heavily industrialized, and in which large amounts of fossil fuels are burned, would be expected to have greatest exposure from ambient sources of fluoranthene. In addition, certain occupations (e.g., coke oven workers, steelworkers, roofers, automobile mechanics) would also be expected to have elevated levels of exposure relative to the general population.

Exposure to fluoranthene will be considerably increased among tobacco smokers or those who are exposed to smokers in closed environments (i.e., indoors).

Basis and Derivation of Criterion

The attempt to develop a valid drinking water standard for fluoranthene is hindered by several gaps in the scientific data base:

(1) There have been no chronic dose-response studies conducted with fluoranthene in animals.

(2) There are no chronic animal toxicity studies involving oral exposure to fluoranthene.

(3) There are no human data concerning the effects of exposure to fluoranthene.

However, assuming that the development of a standard must proceed despite these obstacles, several approaches may be attempted. Taking the existing World Health Organization recommended standard of 0.2 µg/l for PAH's in drinking

water, one can ask what proportion of that amount is represented by fluoranthene.

From a survey of PAH's in U.S. drinking waters using the same criteria for analysis as recommended by the World Health Organization, it is possible to calculate the amount of fluoranthene relative to other PAH's in the same sample (Saxena, et al. 1977; Basu and Saxena, 1977-78). These data indicate that in drinking water samples where fluoranthene was detected, it represented about 58.9 percent of the total PAH's. Therefore, a drinking water standard for PAH's at 0.2 µg/l would be equivalent to a drinking water standard for fluoranthene of:

$$0.2\ \mu g/l \times .589 = 0.12\ \mu g/l$$

Attempts to develop a drinking water standard based upon animal toxicity data are seriously hindered by an inadequate data base. The only study available which shows a no-effect level for fluoranthene (in terms of chronic mortality) was reported by Hoffmann, et al. 1972). This study involved dermal administration of fluoranthene to mice, and necessitates the assumption that 100 percent of the applied dose was absorbed. Their data can be used to develop a drinking water standard based on the method employed by the U.S. E.P.A. in formulating national interim primary drinking water regulations (U.S. EPA, 1976).

Calculation of the criterion is summarized in Table 14 below. The approach taken was to take into consideration the contribution of dietary and airborne sources of fluoranthene. Once these factors are accounted for, this procedure

TABLE 14

Derivation of Criterion for Fluoranthene in Water

Species	Chronic No-effect Level	mg/kg body weight/day[a]	Calculated Maximum Safe Levels			Intake from:		Maximum Permissible Intake from Water	Recommended Limit
			Safety Factor (x)	mg/kg/day	mg/man/day[b]	Diet mg/man/day[c]	Air mg/man/day[c]	mg/day	µg/l
Mouse (Ha/ICR/Mil Swiss Albino	50 µl of 1.0% fluoranthene in acetone applied 3 times weekly for 12 months	6.12	1/1000	.006	.420	.016	.0001	.400	200 µg/l

[a]Assume weight of mouse = 35 grams

[b]Assume average weight of human adult = 70 kg

[c]Calculated as described above in text

[d]Assume average daily intake of water for man = 2 liters.
Calculation based on assumption that water accounts for 0.1% of total exposure

leads to the conclusion that 200 µg/l of fluoranthene in drinking water would represent an acceptable level of exposure. It must be emphasized, however, that the criterion is based on chronic toxicity data with mortality being the endpoint, and applies only to situations where exposure occurred to fluoranthene alone. In environmental situations, it is well established that fluoranthene is found in the presence of numerous PAH's; a situation having important implications for potential toxic interactions.

Several studies have clearly shown that fluoranthene possesses no carcinogenic activity, and is neither a tumor initiator nor a tumor promoter (see Carcinogenicity section of the document). However, two carefully conducted studies have shown that fluoranthene, when applied to mouse skin together with much smaller quantities of benzo(a)pyrene, could act as a cocarcinogen to increase tumorigenic response. These data do not permit a quantitative estimation of health risks incurred by this type of biological phenomenon. Nevertheless, because fluoranthene is present in environmental mixtures together with other PAH's (including several carcinogens) it may pose an additional risk to the population exposed. In view of the cocarcinogenic and anticarcinogenic properties of several environmental PAH's, the degree of added risk, if one exists, cannot be easily determined on the basis of our present scientific knowledge.

Inadequacies in the current scientific data base prevent the formulation of a drinking water criterion for fluoranthene based on potential cocarcinogenicity. However, it would

seem prudent to temporarily limit the level of fluoranthene in drinking water to no more than the acceptable concentration of the sum of all non-fluoranthene PAH's. In addition, since environmental exposures to fluoranthene will almost certainly involve concomitant exposure to carcinogenic PAH's, their potential interaction should be considered in future research and health criteria development.

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